REMARKS

Claims 1-29 and 70-83 are pending. Claims 30-69 have been cancelled. Claims 1-4, 9, 10, 12, 13 and 15-29 have been amended. Claims 70-83 have been added. Support for the new claims and amendments can be found throughout the application as originally filed. No new matter has been added.

Rejection of Claims 3-14 and 18-23 Under 35 U.S.C. §112, second paragraph

Claims 3-14 and 18-23 are rejected under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

In particular, the Examiner rejected claim 3, and the claims depending therefrom, based upon the term "portion thereof". Claim 3 has been amended to remove this term, thereby obviating this rejection.

Claim 4, and the claims that depend from claim 4 are also rejected by the Examiner based upon the "recitation of the terms 'substitutions' and 'combinations'." Specifically, the Examiner states that "it is unclear as to which substitutions or combinations the applicant is referring. There are numerous possible substitution or combinations that are possible and because the claims do not specifically limit the types or actual substitution or combination, the metes and bounds of the terms cannot be determined."

Applicants have amended claim 4 to remove the term "combinations thereof", thereby obviating the rejection with regard to this language. With regard to the term "substitutions", Applicants respectfully traverse this rejection. Contrary to the Examiner's assertion, the claims do specifically limit the types of substitutions. The claims recite that the substitutions are conservative substitutions. In addition, claim 4 as amended recited that the MUC1-specific binding partner binds MUC1. Therefore, the types of substitutions are further limited by the claim language to those that retain the MUC1 binding capabilities of the binding member. Thus, the metes and bounds of the term "substituted sequences" is clear from the language of claim 4. Therefore, Applicants respectfully request that the Examiner withdraw this rejection.

The Examiner also rejected claims 18-23 "in the recitation of the term 'about' is a relative term that the specification has not adequately defined."

Applicants respectfully traverse this rejection. Contrary to the Examiner's assertion, the term "about" in claims 18-23 is definite. The term "about" has clear meaning—it means amino acid sequences having the specified percentage of homology as well as percentages close to the specified percentage. The courts have held that the term "about" has clear meaning. See, e.g., *Ex parte Eastwood*, 163 U.S.P.Q. 316 (Bd. App. 1968), which provides that "the term 'about' used to define the lower end of a mold as between 25 to about 45% of the mold entrance was held clear, but flexible." Therefore, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection of Claims 3-29 Under 35 U.S.C. §112, first paragraph

Claims 3-29 are rejected under 35 U.S.C. §112, first paragraph "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner states that

> The written description for this case has only set forth MUC1-specific binding members defined by specific sequence identification numbers and therefore the written description is not commensurate in scope to claims that read on antigen binding members of having the formula represented by portions of sequences, substitutions of sequences, combinations of sequences, sequences that are 70%, 80%, 90%, 95%, 97% and 99% homologous.

The term portions thereof has been removed from the claims, thereby obviating this portion of the rejection. With regards to MUC1 binding members having substitutions or homology to the sequences, Applicants respectfully traverse this rejection. The claims are directed to MUC1-specific binding members that bind MUC1 and include a recited sequence, high homology to the recited sequence or conservative substitutions of the recited sequence.

The claimed binding members are required to have structural features, namely the recited sequence or a high level of homology to the recited sequence, and the functional property of

binding MUC1. All of the sequences recited in claims 3-25 are about 17 amino acids in length or less. Therefore, the levels of homology recited in the claims only allows for a very small number of changes. For example, the amino acid sequence of residues 31-35 of SEQ ID NO:3 is only 5 amino acids in length. That means an amino acid sequence that is 80% homologous to that sequence can only differ by one amino acid. Claims 26 to 29 include longer sequences (e.g., an amino acid comprising SEQ ID NO:1 or SEQ ID NO:3). However, these claims require a higher level of homology, namely 90% or more, plus the functional limitation of binding MUC1. Applicants have described the various sequences and pointed to hot spots within these sequences that may confer high affinity to MUC1. See, e.g., page 56 of the application. With regard to the amino acid sequence of residues 99 to 110 of SEQ ID NO:3, Applicants have further demonstrated at least 5 different residues that can be changed and have provided specific amino acid residues that can make up those changes. Thus, Applicants have provided more than one species of the limited genus of binding members of the claims. Therefore, based on the disclosure in the present application, a skilled artisan could envision the structure of the claimed binding members and could easily determine if such binding members had the requisite MUC1 binding activity.

A similar situation is described in Example 14 of the "Synopsis of Application of the Written Description Guidelines" (hereafter referred to as "the Synopsis"). The claim in that example recites a protein having at least 95% homology to a recited sequence and having the ability to catalyze a particular reaction. Only one sequence is disclosed. Like the present claims, the claim in the example includes variants ***but*** all variants must possess the specified activity and must have at least the specified level of homology to the sequence. The Synopsis states that "the single species disclosed is representative of the genus" and that there is sufficient written description of the genus in this scenario. One of the main differences between this example and the claimed invention is that because the sequences recited in most of the claims are so small, fewer changes are allowed by level of homology recited in the claims than would be allowed for a sequence having 95% homology with a full length protein sequence. In addition, the present application discloses more than one species covered by the claims. Thus, the genus of sequences

covered in many of the claims is smaller than the genus acknowledged by the USPTO in the Synopsis to have sufficient written description.

Contrary to the Examiner's assertions, the level of homology required by the claims covers a fairly small number of changes to the recited sequences. In addition, the present application describes these various sequences and provides direction regarding amino acids important to retain activity. The claims also require that the binding member bind MUC1. Thus, the claims provide both structural and functional limitations. In view of the relatively small number of sequences that are covered by the claims and the disclosure in the present application, it is clear that there is written description for the claimed binding members.

Claims 15-17 are also rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification is such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Specifically, the Examiner states that

> It is apparent the cell lines are required to practice the claimed invention because they are specifically required in the claims. As required elements they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements ... may be satisfied by a deposit of the cells lines.

Applicants respectfully traverse this rejection. Contrary to the Examiner's assertion, the DP47 and DPK15 germ line sequences were readily available to the public at the time of filing. For example, as provided at page 34 of the specification, the DP47 and DPK15 germline sequences were available, and accessed by the Applicants, at the Sanger Center Sequence database. In addition, Applicant provides herewith Exhibits A and B. Exhibits A and B are Genebank data sheets that provide the DP47 and DPK15 germline sequences and indicate that such sequences were available on Genebank prior to the priority date of the present application. Applicants also submit herewith Exhibits C & D which are references published in the early

1990's disclosing these sequences. In view of the teachings of the application and the evidence provided herein, it is clear that the DP47 and DPK15 germline sequences were readily available to the public at the time of filing. As such, a skilled artisan would be able to make and use the inventions of claims 15 to 17 without undue experimentation.

For the reasons discussed above, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection of Claims 4-8 and 18-29 Under 35 U.S.C. §102(b)

Claims 4-8 and 18-29 are rejected under 35 U.S.C. §102(b) as being "anticipated by Arathoon R et al (WO 98/50431)." In particular, the Examiner states that

> Claims are drawn to a MUC-1 specific binding member wherein the antigen binding domain comprises a CDR comprising an amino acid sequence selected from the group which includes amino acids 50-66 of SEQ ID NO:3. ... Arathoon R et al. teach a multispecific antibody that comprises amino acids 50-66 of SEQ ID NO:3 and further discloses making a single chain Fv and or a multispecific antibody that comprises this sequence. ... Because the amino acid sequence taught by Arathoon R et al is identical to amino acids 50-66 of SEQ ID NO:3, it reads on sequences that are 70-99% homologous to any one of the sequences taught in claims 1-4, specifically amino acids 50-66 of SEQ ID NO:3.

Applicants respectfully traverse this rejection. The claims are directed to MUC1-specific binding members and polypeptide molecules that bind MUC1 and include a recited sequence, high homology to the recited sequence or conservative substitutions of the recited sequence.

Arathoon et al. disclose a bispecific antibody that binds Ob-R and Her3 having one of the recited amino acid sequences. As provided at page 9 of the Arathoon reference, a bispecific antibody is an antibody that binds only two antigens. Thus, Arathoon et al. disclose an antibody that binds only Ob-R and Her3. In addition, there is nothing in the Arathoon reference that points to the particular portion of the entire sequence disclosed. Therefore, Arathoon et al. does

not teach or suggest every element of the claimed invention, and thus, does not anticipate the claims.

Claims 4, 8 and 18-29 are further rejected under 35 U.S.C. §102(b) as "being anticipated by Kanappik A et al. (WO 97/08320)". Specifically the Examiner states that

> Kanappik A et al. teach an amino acid sequence that is identical to that of amino acids 31-35 of SEQ ID NO:3 and further teach of using the amino acid sequences as part of a single chain Fv antibody, and Fab fragments. Because the amino acid sequence taught by Kanappik A et al is identical to amino acids 31-35 of SEQ ID NO:3, it reads on sequences that are 70-99% homologous to any one of the sequences taught in claims 1-4, specifically amino acids 31-35 of SEQ ID NO:3.

Applicants respectfully traverse this rejection. Kanappik et al. disclose methods of making artificial antibodies by piecing together various portions from any known germline sequence. The Kanappik et al. reference provides over 150 pages of sequences and provides a list of hundreds of germ line sequences. Nothing in that reference teaches or suggests selecting the particular sequence recited in the claims from all of the disclosed sequences. In addition, there is no mention whatsoever of MUC1 or MUC1 binding capabilities in the Kanappik reference-forget that a particular sequence could have MUC1 binding capabilities. Thus, Kanappik et al. does not teach or suggest every element of the claimed invention, and thus, does not anticipate the claims.

Claims 1 and 2 are rejected under 35 U.S.C. §102(b) as "being anticipated by Brugger et al. (J Clin Oncol 1999 May 17(5):1535-44)." The Examiner asserts that

> Claims 1 and 2 are drawn to an isolated MUC-1 binding member comprising an antigen binding domain. Brugger et al disclose an antibody that is able to bind the MUC-1 protein. Since it cannot be determined from the recited claims what the actual sequence claimed is, the claims read on any antibody capable of binding the MUC-1 antigen.

Applicants respectfully traverse this rejection. The Examiner's assertion that the actual sequences claimed cannot be determined from the claims is simply not true. The claims

specifically recite a sequence that the MUC1 binding member must include and therefore, read only on antibodies that include at least one of the recited sequences. Thus, the claims read on any antibody that binds MUC1 ***and*** includes a recited sequence.

The claims, as amended, also recited that the amino acid sequence is in its original germline framework or is in a framework of a different polypeptide.

Brugger et al. disclose various MUC1 antibodies, all of which are murine antibodies. Therefore, none of the antibodies disclosed by Brugger et al. are in a germline framework or in a framework from a different polypeptide. Instead, the murine antibodies disclosed by Brugger et al are in their original murine framework. Therefore, Brugger et al. do not teach or suggest every element of the claims, and thus does not anticipate the claimed invention.

Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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